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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/710,760	11/10/2000	John C. Royer	5563.210-US	5635
25907	7590	10/06/2003	EXAMINER	
NOVOZYMES BIOTECH, INC. 1445 DREW AVE DAVIS, CA 95616			MARVICH, MARIA	
			ART UNIT	PAPER NUMBER
			1636	18

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/710,760

Applicant(s)

ROYER ET AL.

Examiner

Maria B Marvich, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 90-100 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 90-93 is/are allowed.
- 6) ☒ Claim(s) 94, 97-100 is/are rejected.
- 7) ☐ Claim(s) 95-96 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 October 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

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DETAILED ACTION

This Office Action is in response to an Amendment filed 5/12/03, Paper No. 16. Claims 101 and 102 have been canceled. Claims 90-100 are pending in this application. A new ground of rejection is found herein and, therefore, this rejection is Non-Final.

Drawings

Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

Claim Objections

Claims 95 and 96 are objected to under 37 CFR 1.75 as being substantial duplicates of claim 94. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). It is unclear that the trichodiene synthase of claim 94 from *Fusarium venenatum* strain ATCC 20334 differs from the trichodene synthase encoded by SEQ ID NO: 1 and from the trichodiene synthase contained in pTri5. SEQ ID NO: 1 and pTri5 are both obtained from *Fusarium venenatum* strain ATCC 20334 and therefore should be the same trichodiene synthase of claim 94 from *Fusarium venenatum* strain ATCC 20334.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 94 and 100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **In the office action filed 10/21/02, Paper No. 14, the rejection of claims 85 and 89 for the same reasons as above was withdrawn. Upon reconsideration, this rejection has been reinstated and applied to claim 100. For purposes of determining Finality of this action, this is considered a New Rejection.**

Since the specific *Fusarium venenatum* cells deposited at ATCC 20334 are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. The invention does not recite use of any cells but instead specifically claims *Fusarium venenatum* cells deposited at ATCC as strain ATCC 20334. The *Fusarium venenatum* cells deposited at ATCC as strain ATCC 20334 are commercially available, however, commercial availability is not necessarily evidence that the public will have access to the material for the life of a patent (see MPEP 2404.01) (emphasis added). Others deposited the *Fusarium venenatum* of the invention, their availability in an unrestricted form for the life of a patent issued on the instant application cannot be ensured. Applicants must therefore deposit the specific *Fusarium venenatum* recited in the claims and thus satisfy the deposit requirement under 37 CFR 1.801-1.809 (see enclosed Suggestion for deposit of biological material).

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Claims 97-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This is a new rejection.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and *In re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) Nature of invention. The invention recites an isolated functional fragment of the trichodiene synthase of SEQ ID NO:2 wherein one or more amino acids are deleted from the amino and/or carboxyl terminus of SEQ ID NO: 2. This invention utilizes disciplines of recombinant technology as well as protein production. As well, assays for "functional" fragments" among the recombinant molecules are required to perform the invention.

2) Scope of the invention. The fragments can have any number of deletions at the N-terminus or C-terminus. Therefore, claims 97-100 recite a broad collection of proteins.

3) Number of working examples and guidance. While the sequence of SEQ ID NO: 2 is taught in the specification, no examples of fragments of trichodiene synthase or what domains or regions are required for function of trichodiene synthase. Therefore, there is no indication of a structure-function relationship between the sequence of SEQ ID NO 2 and trichodiene synthase

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activity. Furthermore, the instant specification fails to demonstrate any examples or specific guidance for the identification or isolation of “functional fragments” of SEQ ID NO: 2, i.e. assays for the analysis of trichodiene fragments that would meet the limitations of the claims. Applicants simply state that using methods known in the art specific for the enzyme with reference to Hohn and Beremand, 1989 on page 31, line 3-8. This reference teaches the primary structure of a trichodiene synthase (TS) gene isolated from *Fusarium sporotrichiodes* (see abstract). This guidance, for the isolation and sequence analysis of trichodiene synthase genes is provided in the specification. However, no guidance is given for the isolation of “functional” fragments of trichodiene synthase **protein**.

4) State of the art. Recombinant technology for the generation of new protein fragments is highly developed. However, the ability to determine *a priori* whether a mutation will generate a functional fragment is not. The art must therefore be considered to be poorly developed.

5) Unpredictability of the art. Without knowing the structure-function relationship of SEQ ID NO:2, the ability to predict the effect of mutations on function is highly unpredictable.

6) Amount of Experimentation Required. The invention recites isolated functional fragments of trichodiene synthase. In view of the unpredictability of the art of predicting the functional nature of fragments of SEQ ID NO 2 deleted of any number of amino acids from the C-terminus and/or the N-terminus: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the unpredictability of the art, the poorly developed state of the art with regard to predicting the structural/ functional characteristics of a protein from primary amino acid sequence alone, the lack of working examples and the lack of guidance

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provided by applicants, the skilled artisan would have to have conducted undue, unpredictable experimentation to practice the claimed invention.

Claims 97-100 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained from reasons of record in the office action filed 10/21/02, Paper No. 14 and restated below.**

Claim 97 is drawn to an isolated functional trichodiene synthase of SEQ ID NO: 2 wherein one or more amino acids are deleted from the amino and/or carboxyl terminus. Therefore, applicants claim a genus of functional trichodiene synthase molecule with any amino and/or carboxyl terminal deletions.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus. In the instant case, applicants teach full-length trichodiene synthase from *Fusarium venenatum*. Applicants do not teach any fragments of trichodiene synthase or what domains or regions are required for functional trichodiene synthase. Therefore, there is no disclosure of a structure-function

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relationship between the sequence of SEQ ID NO 2 and trichodiene synthase activity. Given the large size and diversity of fragments generated by deletion at the N and/or C-terminus and the inability to determine which will also have the essential element, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Response to Argument

Applicants traverse the claims rejection under 35 U.S.C. 112, deposit requirement on pages 4-5 in the amendment filed 8/5/02, Paper Number 13. Applicants argue that the ATCC 20334 strain is "known and readily available" and therefore need not be deposited. 37 C.F.R. 1.802(b) as set forth at page 232 of 1122 Official Gazette 223-38, states "Although there is a public interest in the availability of a deposited biological material during and after the period of enforceability of the patent, the examiner need not be unduly concerned about continued access to the public. Unless there is a reasonable basis to believe the biological material will cease to be available during the life of the patent, the examiner should accept current availability as satisfying the requirement." Applicants argue that due to the ATTC catalog listing of *Fusarium venenatum* cells ATCC 20334, *Fusarium venenatum* cells deposited at ATCC 20334 are preserved and are currently available to the public.

Applicants' arguments filed 8/5/02 have been fully considered but they are not persuasive. MPEP 2404.01 states that the biological material must be "known and readily available"- neither concept alone is sufficient. Strain ATCC 20334 is a commercially available

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strain but may not be readily available should the original depositors withdraw the cells from the open collection. As the applicants are not the original depositors and the availability of *Fusarium venenatum* cells ATCC 20334 is not known and readily available by other means, there is a reasonable basis to believe that the biological material will cease to be available during the term of the patent. Public access during the term of the patent may affect the enforceability of the patent. The applicants cannot guarantee the commercial availability of the cells for the life of the patent unless they deposit the cells themselves.

Applicants traverse the claims rejection under 35 U.S.C. 112, first paragraph, written description on pages 1-3 in the amendment filed 5/12/03, Paper Number 16. Applicants argue that the function of trichodiene synthase is "trichodiene synthase" and the structure is "SEQ ID NO:2. Furthermore, applicant argues that the fragments involve simply removing one or more amino acids from the amino or carboxy-terminus of SEQ ID NO:2. Furthermore, applicants submit that claims to such fragments are allowable subject matter in US patents 6,221,644 and 6,372,464 and 6,489,154.

Applicants' arguments filed 5/12/03 have been fully considered but they are not persuasive. As applicants are deleting amino acids from the N and/or C terminus of SEQ ID NO:2, the structure-function relationship of the isolated fragments will not be the same as that of SEQ ID NO:2. While the function of SEQ ID NO:2 is understood to be trichodiene synthase, the ability to determine which of the fragments generated by the deletion of amino acids from the N and/or C-terminus is also functional is highly unpredictable due to the lack of guidance in the specification and prior art of record. The simple deletion of amino acids at the C and/or N-terminus has the potential to generate a broad genus of fragments. The specification does not

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reduce to practice the ability to determine which fragments will also be "functional". It is reminded that while the cited cases, 6,221,644, 6,372,464 and 6,489,154 (which teach respectively lipase, peroxidase and lisophospholipase) teach identification of fragments of the respective proteins, each application is reviewed on its own merits.

Conclusion

Claims 90-93 are allowed.

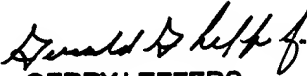
Claim 94 and 97-100 are rejected.

Claims 95-96 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


GERRY LEFFERS
PRIMARY EXAMINER

Maria B Marvich, PhD
Examiner
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September 26, 2003